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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/580,476	05/26/2000	Edwin G. Westaway	37264.6.0	8898

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EXAMINER
GUZO, DAVID

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 02/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/580,476	WESTAWAY ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 22 November 2002.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 2-5, 7-9, 15-25, 33-42 and 49-65 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 2-5, 7-9, 15-25, 33-42 and 49-65 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 5/26/00 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☒ Other: Attachment on Deposit of Biological Materials

Detailed Action

The indicated allowability of claims 40-42 is withdrawn in view of the following new grounds of rejection.

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 2-5, 7-9, 15-25 and 33-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim a gene expression and delivery system comprising a replicon derived from the Kunjin virus (a flavivirus) wherein the replicon is encapsidated in a virus-like particle (VLP) which can be made up of any structural proteins. The claims therefore read on a genus of gene expression and delivery systems comprising sequences necessary to encapsidate a Kunjin viral or Kunjin virus derived replicon in infectious virus-like particles. Applicants have provided a description of a Kunjin virus gene expression and delivery system wherein the Kunjin viral

replicon is encapsidated in Kunjin viral structural proteins (prM, E and C proteins).

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

In the instant case, applicants provide an example of recombinant Kunjin viral particles comprising a Kunjin viral replicon encapsidated within Kunjin viral structural proteins. Applicants provide no disclosure of flaviviral-like particles comprising Kunjin viral replicons encapsidated within any other viral or non-viral structural proteins. Applicants provide no disclosure of what other proteins would be capable of encapsidating Kunjin viral replicons in "viral-like particles" or "flaviviral-like particles". Applicants provide no correlation between the structure of the Kunjin viral structural proteins and their function of being able to package Kunjin viral nucleic acids (replicons) into viral particles and it is unclear what structural features would need to be present in other proteins which would enable them to function as structural proteins that can encapsidate Kunjin viral replicons. Given the broad scope of the invention (reading on any flaviviral, viral or non-viral proteins capable of encapsidating a Kunjin viral

replicon), the diversity of the proteins contemplated by the claims and the absence of a disclosed correlation between the structure of the Kunjin viral structural proteins and other proteins which would function to encapsidate the recited replicons, it must be concluded that the disclosure of a single example using Kunjin viral structural proteins cannot be considered to be a representative number of species sufficient to convince the skilled artisan that applicants were in possession of the claimed genus.

Claims 22-23 and 37-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants claim a gene expression system derived from the specific viral clones FLSD and FLSDX. Applicants claim 18 specific replicons in claims 23 and 40. Applicants claim specific vectors SFV-C, SFV-prME, SFV-prME-C and SFV-prME-C105 in claims 37-39, respectively, and cells stably transformed (with the vectors of claim 40) in claims 41-42. The viral clones FLSD and FLSDX are essential for practicing the claimed invention but the instant specification does not provide a reproducible method for generating these specific clones and the prior art likewise does not disclose these clones. A deposit of these clones is therefore necessary

to guarantee their availability for the life of a patent emanating from the instant application. The specific replicons recited in claims 23 and 40 and the vectors recited in claims 37-39 likewise must be deposited because the instant specification does not provide the skilled artisan with the teachings necessary to exactly duplicate these replicons and vectors and the prior art does not teach them or provide the skilled artisan with the guidance to exactly duplicate these vectors. For example, applicants use PCR to amplify specific regions of Kunjin viral nucleic acids but do not teach the specific primers used in the PCR amplification. Also, applicants rely on the prior art plasmids used in the construction of the plasmid pAKUN (disclosed by Khromykh et al., J. Virol., 1994) for the generation of infectious Kunjin RNA, but the prior art does not teach the sequence of the plasmids used to construct pAKUN or the sequence of pAKUN. Furthermore, it is unclear if plasmids use by Khromykh et al. are currently available or would be available for the life of any patent issuing from the instant application. It is noted that applicants are claiming the precise vectors and replicons and not functional equivalents of said constructs; therefore the skilled artisan would need to be able to reproducibly generate the **exact same vectors and replicons nucleotide-by-nucleotide**.

Claims 2-5, 7-9, 15-25 and 33-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a gene expression and delivery system

comprising a replicon of the Kunjin virus and a second vector capable of expressing Kunjin viral structural proteins, cell lines stably transformed with the Kunjin replicon, methods producing said cell lines, methods of producing Kunjin particles and DNA based Kunjin virus replicon vectors, does not reasonably provide enablement for a Kunjin viral gene expression and delivery system comprising a second vector capable of expressing any flaviviral or any viral or non-viral protein(s) sufficient to encapsidate a Kunjin viral replicon. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is whether the skilled artisan could make and use the claimed invention from the teachings of the application coupled with information in the art without undue experimentation (United States v. Telectronics, Inc., 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based upon a single factor, but instead is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

1) Unpredictability of the art. The art in the area of flaviviral expression vectors is unpredictable. The flaviviral group of viruses is comprised of a large number of poorly characterized viruses, most of which have not been genetically manipulated with regard to generation of recombinant

expression systems. While flaviviruses share some common features with regard to genome organization, they share little sequence homology. The packaging mechanisms for flaviviral RNAs were unknown at the time of applicants' invention. Applicants provide no guidance on what viral or non-viral proteins, other than Kunjin viral structural proteins, could encapsidate Kunjin replicons so as to generate viral like particles and therefore the skilled artisan would be left to practice trial and error experimentation, with no guidance from applicants, in the designing of packaging systems to encapsidate the recited Kunjin replicons. Additionally, if the skilled artisan would attempt to use other flaviviral proteins to encapsidate the Kunjin viral replicons, it is noted that many flaviviral proteins can be cytotoxic to cells and the skilled artisan would need to develop cell lines which could support replication of Kunjin viral replicons and expression of flaviviral proteins necessary to complement *in trans* the Kunjin viral structural protein encoding sequences in the Kunjin replicons.

2) State of the art. The state of the art with regard to the generation of recombinant flavivirus expression vectors and replicons is poorly developed. Most studies published prior to applicants' invention involved research directed to constructing infectious clones of various flaviviruses and identifying flaviviral sequences which could be provided *in trans* to complement the same sequences deleted in deletion mutant flaviviral genomes (See Khromykh et al., J. Virol., 1994, pp. 4580-4588; Galler et al., Brazilian J. Med. And Biol. Res., 1997, pp. 157-168, etc.; all cited

by applicants).

3) Number of working examples. Applicants present working examples only using Kunjin viral replicons encapsidated in Kunjin viral structural proteins so as to form virus like particles.

4) Scope of the claims. The claims are broad and read on Kunjin viral replicons encapsidated in any viral or non-viral proteins so as to form virus-like particles.

5) Amount of guidance provided by applicants. Applicants provide no guidance on the generation of Kunjin viral replicons encapsidated in non-Kunjin viral structural proteins.

6) Nature of the invention. The invention involves a complex and poorly understood area of molecular biology; the generation of recombinant flaviviral gene expression and delivery systems wherein a flaviviral (Kunjin viral) replicon is encapsidated in proteins which are not native to the virus sequences being encapsidated.

7) Level of skill in the art. The level of skill in the art is high; however, given the unpredictability of the art, the poorly developed state of the art, the lack of guidance provided by applicants and the broad scope of the invention, it must be considered that the skilled artisan would have had to have conducted trial and error experimentation in order to attempt to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that the skilled artisan

would have had to have conducted trial and error experimentation in order to practice the claimed invention. Said experimentation must be considered to be undue and excessive.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-5, 7-9, 15-25, 33-39 and 49-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 21, 43, 44, 48, 49, 55 and 65 (and dependent claims) are vague in the recitation of a replicon or vector "...adapted to receive at least a nucleotide sequence...". The metes and bounds of the claimed subject matter are unclear because the "at least" language leaves the claim open to inclusion of undisclosed non-nucleotide molecules into the vector or replicon. Possibly applicants mean to recite "at least one nucleotide sequence".

Claims 20-22, 25, 33-34 and 64 (and dependent claims) are vague in the recitation of vectors or replicons "derived from" Kunjin virus or from an alphavirus such as Sindbis virus, etc. It is unclear how closely related the claimed vectors or replicons are to the original starting materials; for example, in claim 21, how closely related is the claimed replicon to the Kunjin virus from which it was derived? The construction of the replicon can involve deletion and

substitution of some, if not 99.9%, of the Kunjin viral sequences.

In claims 21 and 65, applicants recite "...region and or a protein(s)...". This language is confusion because it is unclear if applicants mean to claim the elements with "and" or "or". Redrafting the claims to recite "and/or" would be remedial.

Claim 17 is vague in the recitation of the phrase "...incorporating corresponding bacteriophage promoters..." because it is unclear what bacteriophage promoters are being referred to; i.e. promoters corresponding to what?

Claims 35-36 are vague in that it is unclear if the sequences from the E protein, the nonstructural region and the 3'UTR are from the Kunjin virus or some other virus.

Claim 39 is vague in that applicants recite that the "...second vector is SFV-prME-C **and** SFV-prME-C105." It is unclear how the second vector can be both of the recited vectors simultaneously. Redrafting the claim to delete "and" and substitute "or" would be remedial.

Claim 50 is vague in that there is no antecedent basis for the term "the eucaryotic expression promoter" in claim 65.

Claim 65 is vague in that there is no antecedent basis for the term "...the complementary DNA sequence of Kunjin virus origin..." in the claim. Also, Kunjin is misspelled as "Kunin" in line 6.

Miscellaneous:

Sequences in the specification must be identified by the appropriate SEQ ID NO: identifiers.

In the specification, on pages 9 and 13-14, the holes punched at the top of the pages have deleted text on the first line of each page. Substitute pages 9 and 13-14 are required. A submission of substitute pages must be accompanied by a statement that the substitute pages contain no new matter.

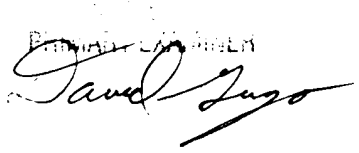
No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Faxes may be sent directly to the examiner at (703) 746-5061.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David Guzo
January 29, 2003



ATTACHMENT

SUGGESTION FOR DEPOSIT OF BIOLOGICAL MATERIAL

A declaration by applicant or assignee, or a statement by applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection based on a lack of availability of biological material. Such a declaration:

1. Identifies declarant.

2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready availability thereto by the public if a patent is granted. The depository is to be identified by name and address (See 37 CFR 1.803).

3. States that the deposited material has been accorded a specific (recited) accession number.

4. States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent (See 37 CFR 1.808(a)(2)).

5. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 CFR 1.14 and 35 USC 122 (See 37 CFR 1.808(a)(1)).

6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer. See 37 CFR 1.806.

7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United

States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, name and address of the depository, date of deposit and the complete taxonomic description.